that, overall, these 2 regimens allows similar reduced TRM and high one-year OS for hematological malignancies and could be selected for further phase III comparison with myeloablative regimen. Further details of sub-group analysis (disease status; acute leukemia, NHL and MM) will be presented in order to assess this conclusion in specific situations with a median study follow-up of 44 [6 – 78] months.

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APPLICATION OF SECOND GENERATION TYROSINE KINASE INHIBITORS IN BCR-ABL POSITIVE MALIGNANCIES IN THE POST-TRANSPLANT PERIOD

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Due to the shift of allogeneic stem cell transplantation (SCT) to poor risk cases in chronic myeloid leukemia (CML), therapy of relapse after SCT is highly relevant. In contrast to Imatinib (IM), where application in stem cell recipients was investigated in many studies, studies on 2nd generation tyrosine kinase inhibitors (TKIs) in the post-transplantat period are limited. We performed evaluation of 25 stem cell recipients with CML and 13 with Phil positive ALL (Phi^+ALL). 9 of those pts received 2nd generation TKIs in the post-transplant period (CML blast phase; BP: n = 6; CML accelerated phase; AP: n = 2; Phi^+ALL; n = 1). There were 5 males and 4 females (median age 54 years). Before allo-SCT, 7 were in hematological remission, 8 pts were MRD positive. 3 pts had Imatinib resistance conferring mutations (T315I, Y253H, L387F). All pts received unrelated SCT after myeloablative/reduced conditioning. Indications for the post-transplant application of dasatinib were as follows: Phi^+ALL: molecular relapse: n = 1; CML: relapse of BP: n = 2, extramedullary CML relapse with skeletal/cutaneous or central nervous manifestations: n = 4, refractory extramedullary manifestation: n = 1, persisting MRD: n = 1. The median interval between SCT and dasatinib was 7 months (3–19). Before start of dasatinib after SCT, 4 cases had been refractory to imatinib. Starting dose of dasatinib was 2 × 70 mg or 2 × 50 mg. Dose escalation was possible in 3 pts; reduction was necessary in 1 pt. In 1 pt dasatinib was interrupted due to gastrointestinal intolerance/thrombocytopenia. Median treatment duration was 9 months (range 1–17). 3 cases showed response to therapy: 1 pt is in stable major mol. remission, 2 other patients are in partial remission of extramedullary relapse. 1 pt suffers from meningeosis leukemica and receives intrathecal cytarabine. Due to refractoriness, the ALL pt was transferred to nilotinib. 4 pts (44%) died after 6, 7, 9, and 33 months from SCT due to progression. Median overall survival after start of dasatinib was 10 months. In conclusion, although the limited sample has to be considered, it seems that dasatinib can be administered with acceptable tolerance in the post-transplant period and is able to stabilize the situation in single cases of extramedullary or hematological relapse after SCT even in advanced disease and in a poor-risk situation. Future prospective studies should further evaluate the best application schedules of 2nd generation TKIs in the post-transplant period.

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CLINICAL AND COST OUTCOMES OF DOUBLE UMBILICAL CORD BLOOD VERSUS BONE MARROW AND PERIPHERAL BLOOD UNRELATED DONOR HEMATOPOIETIC STEM CELL TRANSPLANTS

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Umbilical cord blood (UCB) is a viable source of hematopoietic stem cells (HSC) however, because of the risk of nonengraftment with low total nucleated cell counts (TNC) per kg, double UCB (DCB) transplants are used in larger patients (pts). We conducted a retrospective review of DCB transplants (n = 30) from January 2004 through April 2008 compared to bone marrow (n = 23, 30%) and peripheral blood (n = 54, 70%) unrelated donor (UD) transplants during the same time period. Median age was 21 yrs (range 13–66) for DCB recipients and 45 yrs (range 0.4–67) for UD pts. UD pts were HLA typed at A, B, C, DR, and DQ and matched with donors at 9(10) (21%) and 10(10) (79%) loci [all mismatches at class I alleles]. DCB recipients had HLA matches of 6/6, 5/6/, 4/6 and 3/6 as follows: (cord 1/ cord 2): (0.0%/6.7%), (20.0%/30.0%), (76.7%/63.3%), (3.3%/0.0%). The median TNC/kg in DCB pts was 2.03×10^7 (range 7.9×10^6 – 9.3×10^8). Median day to ANC>500/ul for DCB and UD pts was 23 days (range 6–66) and 15 days (range 7–52), and platelet >20,000/ul was 52 days (range 7–130) and 19 days (range 9–63), respectively. Incidences of acute GVHD ≥2 and chronic GVHD in the UD and DCB pts were 61.0% and 51% vs. 53.3% and 45%, respectively. Median follow-up was 143 days (range 12–847) for the DCB group and 242 days (range 34–1506) for the UD pts. Estimated overall survival (OS) at 1 year was 61% (95% CI: 48% to 71%) for UD pts vs. 55% (95% CI: 34% to 72%) in DCB pts (p = NS). Estimated transplant related mortality (TRM) at 100 days for UD pt was 6.5% (95% CI: 2.8% to 14.9%) and 16.7% (95% CI: 7.3% to 35.5%) (p = 0.09) in DCB pts. All facility transplant related costs were reviewed from the transplant center thru the first year post transplant, excluding pretransplant workup and care not received at the transplant center. The total median costs for DCB transplants were significantly more than the UD costs at D30, D100 and 1yr post transplant by differences of $42,067, $50,806, and $52,297, respectively (p<0.05 for each time interval). The median length of stay for initial hospitalization at start of preparative regimen was 22 days (2–144) in the UD pts and 29 days (6–103) in the DCB pts, and 60% of total median costs occurred by D30 in the DCB group compared to 52% in the UD group. In conclusion, DCB provides a viable option for HSC with comparable clinical outcomes to UD transplants, however DCB transplants are more expensive primarily because of inpatient costs in the first 30 days.

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BUILDING AN ETHNICALLY DIVERSE CORD BLOOD INVENTORY: A SINGLE INSTITUTION'S INITIATIVE TO INCREASE AFRICAN AMERICAN DONATIONS

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In 2005, the United States Congress passed the Stem Cell Therapeutic and Research Act. A central component of this legislation was the development of the National Cord Blood Inventory (NCBI). A competitive bidding process was instituted and to date three cohorts of banks have been funded with the charge to collect and store 150,000 new cord blood units. A goal in the development of this new inventory is to increase the number of cord blood units from underrepresented racial and ethnic groups. The St. Louis Cord Blood Bank (SLCBB) began participating in this program in September of 2007. The focus for our bank in achieving the goal of diversification was to establish strategies for recruiting African American donors. Historically, this ethnic group has not widely participated in cord blood donation in the St. Louis area. A pilot study was instituted by the SLCBB at SSM St. Mary's Health Center in October of 2007. This hospital was chosen due to its diverse patient population. We hypothesized that the insertion of a dedicated staff nurse into this facility, to educate and communicate directly with potential donors, would result in a significant increase in donations from African Americans. The results from this study are dramatic. A total of 448 cord blood units were collected during the study period (October 1, 2007 – September 30, 2008) as compared to 54 cord blood units during the previous 12 month period (p = <0.0001). This equates to a 730% increase in African American donations. This pilot study demonstrated that the SLCBB initiative was successful not only in increasing the donation rate among African Americans, but also an awareness of the life-saving benefits of cord blood. While donations have increased at a significant

rate, the proportion of these units meeting storage criteria is low. Of the 448 units collected in this study, only 19.2% met banking guidelines as compared to 22.0% for Caucasians, 26.7% for Asians, and 20.0% for Hispanics. African American units not meeting storage criteria were deferred primarily for low volume (54.7%) and total nucleated cell count (25.2%). Acknowledging that biologic factors negatively impact the recovery of nucleated cells from cord blood collected from this population, the SLCBB is currently designing a Phase II study to assess alternative methods to increase collection volumes and cellular yield for African American donors.

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T-CELL ENGRAFTMENT KINETICS FOLLOWING MYELOABLATIVE AND NONMYELOABLATIVE REGIMENS FOR ALLOGENEIC HEMATOPOIETIC TRANSPLANTATION

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Monitoring of T-cell chimerism after nonmyeloablative(NMA) regimens has been used to identify patients at risk for graft rejection, relapse and acute and chronic graft-versus host disease and to determine use and timing of donor lymphocyte infusions. Following myeloablative (MA) transplantation chimerism studies are not considered useful because T-cell engraftment is thought to occur rapidly . We analyzed T-cell engraftment following NMA (fludarabine/TBI) and after MA transplantation generally busulfan-based. T-cell chimerism was studied in 116 patients following MA (busulfan-based in 72) and 99 patients following NMA transplantation between 5/2000 and 11/2007, using STR of CD3+ cells at 30, 60 and 90 days. The estimated median interval to T-cells ≥ 50% donor was 29 days after MA and 27 days after NMA and to T-cells≥90% donor was 42 and 44 days respectively. Comparing only the 72 patients receiving busulfan based MA preparation to the NMA patients, T-cell chimerism≥10% ($p < 0.001$) and ≥50% ($p = 0.029$) occurred more quickly after NMA transplantation. There was no difference ($p = 0.68$) in the interval to≥90% donor T-cells. T-cell chimerism>50% was associated with more acute GVHD ($p = 0.02$), less graft rejection ($p<0.001$) and less relapse ($p = 0.05$) following NMA regimens, while T-cell chimerism>90% was associated with more chronic GVHD ($p = 0.002$). In MA transplants, chimerism>50% and >90% were associated with more acute GVHD ($p = 0.04$, $p = 0.009$), and chimerism>90% was associated with more chronic GVHD ($p = 0.07$). In NMA, multivariate analysis found that patients with AML ($p = 0.02$) and more prior chemotherapy($p = 0.04$) were more likely to reach chimerism>50%, while those with a diagnosis of AML ($p = 0.04$), MDS ($p = 0.002$) or CLL ($p = 0.05$) were more likely to reach chimerism>90%. In MA, multivariate analysis found that patients with more prior chemotherapy ($p = 0.05$) and peripheral stem cells ($p = 0.008$) were more likely to reach chimerism>90%. These data demonstrated that T-cell engraftment occurred more quickly in NMA than MA transplants using busulfan. Factors predictive of T-cell engraftment kinetics were similar in NMA and MA transplantation. The preparative regimen is only one of many factors determining the kinetics of T-cell engraftment. Designation of a regimen as myeloablative does not correlate with more rapid or complete T-cell engraftment.

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PRE-EMPTIVE TREATMENT WITH CIDOFOVIR FOR SYMPTOMATIC BK VIRUS POSITIVE PATIENTS WHO UNDERWENT ALLOGENEIC STEM CELL TRANSPLANT REDUCES THE RISK OF PROGRESSION TO HEMORRHAGIC CYSTITIS

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We have previously demonstrated that Polyomavirus BK associated hemorrhagic cystitis is becoming an increasingly recognized complication of HSCT. Our previously published retrospective analysis demonstrated that BKV was observed in 48% of patients undergoing an allogeneic stem cell transplant and 16% of them developed hemorrhagic cystitis. Based on the recent findings, we designed a prospective protocol for pre-emptive treatment with Cidofovir for symptomatic BK Viruria. 39 patients underwent an allogeneic stem cell transplant from either an HLA-matched sibling or unrelated donor during fiscal year 2008. Patients who manifested urological symptoms received Cidofovir 375mg IV QOW until all symptoms resolved. Out of 39 of these patients, 59% (23/39) developed BK virus infection determined using quantitative real-time PCR assay. Out of these 23 patients, 61% (14/23) received a myeloablative conditioning regimen (Bu/Cy, TBI/Cy) and 39% (9/23) a non myeloablative (Flu/TBI, Flu/Cy/Rituxan, Cy/ATG/TBI, TBIx1, Flu/Mel/Campath, Flu/Cy/TBI). 30% (7/23) became symptomatic and subsequently received Cidofovir 375mg IV QOW which was continued until all symptoms resolved and 71% (5/7) also received Ciprofloxacin. 57% (4/7) had Graft Versus Host Disease and 86% (6/7) were concurrently receiving high dose steroid therapy. 71% (5/7) developed mild hematuria and 29% (2/7) developed small thrombus in the urine. The mean of total Cidofovir doses received was three and the two patients who developed mild hematuria with thrombus received 5 and 6 doses respectively. Bone marrow suppression was noted in three patients who received Cidofovir which was consequently either held or completely discontinued. All 7 patients had complete resolution of symptoms, and none developed any clinical manifestations of hemorrhagic cystitis defined as gross hematuria or the need of continuous bladder irrigation. There was no correlation with symptoms and BK virus PCR titers. In conclusion, pre-emptive treatment of symptomatic BK Viruria with Cidofovir in the allogeneic stem cell transplant setting is safe and effective and potentially prevents the progression to BK virus induced hemorrhagic cystitis.

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GERIATRIC ASSESSMENT (GA) MAY IDENTIFY VULNERABLE OLDER ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION (HCT) RECIPIENTS

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Comorbidity indices and performance status (PS) have been the primary tools used to predict HCT tolerance; however, these tools suffer from poor discriminative capacity. Geriatric Assessment (GA) has found widespread application to assess reduced physiologic reserve (i.e. vulnerability) among elderly adults. We hypothesized that a modified GA would identify vulnerable HCT recipients 50 years and older. We supplemented the standard pre-HCT evaluation (e.g. history, laboratory, PFT's) with a prospective GA integrating multiple geriatric domains. Among 94 patients (pts) 50 years and older, 91 consented to the GA. The median age was 58 (range 50 – 72). Conditioning regimens were primarily fludarabine/melphalan, fludarabine/busulfan, and clofarabine/melphalan with alemtuzumab and tacrolimus for immunosuppression. The comorbidity domain was scored using four tools: Charlson Comorbidity Index (CCI), Kaplan Feinstein Scale (KF), Hematopoietic Cell Transplantation-Comorbidity Index (HCT-CI) and the Cumulative Illness Rating Scale-Geriatric (CIRS-G). Functional domains were estimated by PS, frailty index (FI), and the physical health portion of the short form 36 (SF36-PH) whereas the mental health portion of the SF36 (SF36-MH) measured mental health. Activities of daily living (ADL) and instrumental ADL (IADL) assessed disability. Table 1 describes the results and variation detected by each tool within each geriatric domain. For comorbidity, the CIRS-G was the most sensitive tool as every pt showed comorbidity. Among functional measures, PS was normal (i.e. PS = 0) in most pts (64%). Only 4% had a PS of 2. In contrast, the FI and SF36-PH demonstrated functional limitations in the majority of pts. Specifically, 52% were "pre-frail" (FI of 1 – 2) and 29% were frail (FI of 3–5). Disability by ADL or IADL was rare. A modified GA in older HCT recipients is feasible and may reveal abnormalities in multiple geriatric domains suggesting vulnerability not recognized by a standard evaluation. Ongoing studies will determine the predictive validity of specific domains within the GA.